A Fatal Case of Q Fever in Southern California

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ONLY three fatal cases of Q fever have been reported in the United States since it was first recognized by Dyer[3] as a disease of man in this country.

One of these cases occurred at the National Institute of Health when a laboratory outbreak of 16 cases was experienced in 1940. The autopsy findings and histopathologic study of the case were reported by Lillie, Perrin, and Armstrong.[6] The brief clinical record which these authors gave corresponds very closely to that in the case here reported and is quoted as follows:

"The patient was a white male, aged 59, gardener and incinerator operator. Onset as 'cold' on April 17, 1940. Admitted to hospital on April 22, died on April 25. Had slight productive cough and chest pain on inspiration. Temperature on hospital admission 102° F., 103.5° F. maximum. Dullness over right lung from scapula to base posteriorly, smaller area on left.

"X-ray: 'Pneumonitis' of right lower lobe, less on left.

"Blood: 6,200 white corpuscles, 82 per cent neutrophils and 18 per cent lymphocytes."

Two brothers died in an outbreak of the disease in a packing plant at Amarillo, Texas, in 1945. One of these patients exhibited definite evidence of pneumonia. Autopsies were not performed. Diagnoses of Q fever in these cases were based on the evidence that both patients were part of a group of workers involved in an acute epidemic (55 cases) and the epidemic was confirmed as being Q fever by the finding of strains of *Coxiella burneti* (Derrick) in blood specimens drawn from some of the acutely ill patients[1] and by positive reactions in tests on the blood of convalescent patients.[5]

An account of a single fatal case of Q fever in Australia is given in the annual report of the Director General of Health and Medical Services for the year 1936-1937, but this case was complicated by chronic tuberculosis which, no doubt, contributed to the death of the individual. No other fatal cases appear to be recorded in the Q fever reports from that continent and it is quite evident from the reports that severe cases of the disease are seldom experienced there.

Although many cases of Q fever were reported among American troops in the Mediterranean area and in troops recently returned or returning from that area,[4, 7] no fatalities were observed.

While it has been established that the clinical entity known as "Balkan grippe" is in some cases Q fever, there is no warranty for attempting to relate observations on that disease to Q fever without further confirmation. It is of interest, however, to quote from a publication on this disease by Dennig[2] which states, "The prognosis is very favorable; the death rate for example, in more than 1,000 patients that I saw in 1941, was under 1 per cent." This death rate is not inconsistent with that so far observed in Q fever in the United States.

The report of a fatal case of Q fever in a vigorous man is of exceptional interest. The patient became infected in the Southern California endemic area, where the disease was first recognized by Young.[8] The report of the case is complete with a clinical history, findings in routine laboratory studies, x-ray record, autopsy disclosures and protocols of experimental animals in which a strain of *Coxiella burneti* (Derrick) was established.

CASE REPORT

A 43-year-old Caucasian male, employed at the stockyards in Los Angeles County, California, died December 11, 1947, following an acute illness, diagnosed as influenza, which terminated in pneumonia. Diagnosis of Q fever was established by the presence of the infecting organism in experimental animals inoculated with blood drawn postmortem from the body of the patient.

Clinical findings: The patient worked at his regular duties handling cattle at the stockyards on December 2, 1947, although he had been ill for five to eight days with what he considered to be an ordinary head cold. He stayed home and in bed because of illness on December 3. On December 4, when the temperature was noted to be 103° F., a physician was called. One of the authors (D.B.) first saw the patient on December 4. At that time the temperature was 103° and was reported to have been as high as 105°. The patient complained of frontal headache, malaise, and profuse perspiration. There was a slightly productive cough but percussion and ausculation of the chest did not reveal any obvious lung involvement. The patient had been taking plain empirin compound which partially relieved the headache. He was given 200,000 units of penicillin in oil and wax. One gram of sulfadiazine every four hours and other symptomatic measures were prescribed. The patient remained at home and was told he had epidemic influenza. (Influenza "A" was epidemic in the Los Angeles area throughout the months of November and December, 1947.)

When visited again two days later, the patient was mentally confused and remained so for the duration of the illness. He was coughing frequently and perspiring profusely. The left lower lung area was dull to percussion and showed impaired resonance. Hospitalization was recommended but rejected.

There was no marked change in the patient's condition in the next three days. An x-ray film of the chest taken on December 7 with a portable machine was interpreted as showing "an extensive area of increased density from the base to the second rib on the left side. The extreme upper chest and costophrenic sulcus remain aerated to some degree. The right chest is clear." On December 10, the patient appeared to be slightly cyanotic and oxygen was administered at home. The pulse was 120 to 130 and temperatures were spiking to 105°.

A second roentgenogram of the chest taken in the late afternoon was interpreted as showing "the entire left hemi-

thorax to be homogeneously dense, with evidence of a streaky, patchy, consolidation in the right mid-lung extending from the hilum to the periphery. Findings are consistent with pneumonia of the left chest with rapidly progressive increasing effusion with extension of pneumonitis into the right chest. This could well be viral in type." A few minutes after the exposure, while the film was being developed, the patient experienced a convulsive seizure, with difficulty in breathing, and died.

Laboratory Findings: Routine laboratory studies performed late in the course of illness were not especially informative. Results of urinalysis were reported as follows: color, amber; specific gravity, 1.020; reaction, acid; albumin, 2 plus; sugar, 0; pus cells, 1 to 3 per highpower field; epithelial cells, 1 to 3 per highpower field; granular casts, 1 to 2 per highpower field.

On December 8, blood findings were recorded as follows: hemoglobin was 93 per cent; erythocytes numbered 5,000,000 and leukocytes 5,000 with a differential count of 74 per cent polymorphonuclear leukocytes, 25 per cent lymphocytes, and 1 per cent eosinophils.

SUMMARY OF CLINICAL FINDINGS

The conspicuous findings observed during the patient's illness may be summarized as follows: chills, fever, profuse perspiration, weight loss, frontal headache, mental confusion, nasal congestion and mucoid discharge. There was some aching of the back but it was not a chief complaint. The appetite was poor but there was no indigestion, diarrhea or vomiting. At no time during the illness was cutaneous eruption or jaundice in evidence.

The patient had experienced an appendectomy and a herniorraphy about twelve and ten years previously and had convalesced without complications. He did not use drugs of any sort regularly, and he used alcohol and tobacco (cigarettes) moderately. He had been working overtime for the past few months and had lost considerable sleep. Six feet in height, well-developed and well-nourished, the patient had weighed 190 pounds before becoming ill. There was no known history of disease that would have complicated the present illness.

No diagnosis other than influenza with pulmonary involvement had been made at the time of the patient's death. Q fever was not suspected, as the majority of the medical profession in Los Angeles County was not then familiar with the clinical symptoms of this disease.

AUTOPSY

Autopsy was performed about 40 hours after embalming. Previously, three hours after the body was embalmed, 20 cc. of blood was removed from the left femoral vein for study.

During the embalming operation, poor drainage had been observed and many thrombi, 6 to 8 inches long, had been flushed from the venous system.

The pleural cavity contained several hundred cc. of serous fluid. The pericardium contained an excess of fluid. No sclerosis of coronary arteries was noted.

The lungs presented a somewhat dark edematous mottled appearance with generalized anthracosis. The lung tissue was extremely heavy and consolidated, with the exception of a small area in the right upper lobe that seemed fairly well aerated. This was the only area of lung tissue that appeared to be functioning at the time of death. A roentgenogram, taken immediately before death, showed a large central area in the right lung that was not consolidated. On gross sectioning, the lung tissue was found to be firm and filled with watery fluid. No purulent areas were found. Small whitish areas about 2 mm. in diameter resembling areas of necrosis were evident on the surface and deep in the lung tissue. The larger blood vessels of the lungs were opened at the hilum and a fibrinous clot of almost cartilaginous firmness about 7 to 8 cm. long was found in the artery of the left upper lobe. This did not appear to be of post-mortem formation. The hilar lymph nodes showed no enlargement.

The spleen was not enlarged but was extremely friable. When the capsule was cut through, it presented an appearance resembling that found in acute toxemia. The tissue was soft and oozed out of the cut surface. The organ was dark burgundy in color. The liver appeared normal in size and color.

There were mottled patches on the surface of the kidneys, and an area of hyperemia was noted in the right kidney when sectioned. The capsules were easily removed. No other gross changes were observed in the organs of the thorax or abdomen. The central nervous system was not exposed.

The cause of death was considered to be: (1) Atypical pneumonia; (2) Pulmonary embolism secondary to thrombophlebitis of the femoral veins.

HISTOPATHOLOGIC STUDIES

The tissue specimens for histopathologic study were sent to the Division of Pathology, National Institute of Health, Bethseda, Maryland. A detailed report is being prepared by Dr. Perrin and his associates. For the purpose of this report, we quote his summary comment: "The broncho-pneumonia is consistent in type with that seen in a case of Q fever in this laboratory (National Institute of Health). In some respects, it is not dissimilar to the pneumonia seen in psittacosis and other virus infections."

TESTS ON POST-MORTEM TISSUES

Blood: A portion of the sample removed from the femoral vein was injected into guinea pigs within 30 minutes and the remainder was centrifuged. Serum was saved for complement fixation test and the sedimented cells were resuspended and injected into another guinea pig.

This serum sample was tested with negative results at three separate laboratories which had been testing numerous samples for Q fever by complement fixation tests. (Complement-fixing antibodies are not to be expected early in the acute stage of Q fever infection.)

Sternal tissue: A portion of the sternum was saved for animal injection. This piece, containing much red

marrow and blood, was crushed in a mortar with sterile saline, and a heavy suspension was obtained and was injected into four guinea pigs.

One guinea pig injected with blood showed two days of fever of 40.3° C. and 41.0° C., respectively, and was sacrificed on the 12th day; at autopsy the cutaneous edema and induration characteristic of Q fever in the guinea pig were present. The spleen was enlarged and when spleen tissue was passed to two fresh guinea pigs, infection was produced in them. These two guinea pigs exhibited definite scrotal swelling and reddening which is not common in animals inoculated with *C. burneti*. An abundance of rickettsiae was observed in smears of the subcutaneous exudate.

The other guinea pig injected with blood exhibited a fever of 41° C. on the 13th day and 40° C. on the 14th day after injection. A blood sample taken on the 24th day was positive for Q fever by the complement fixation test at a dilution of 1:64 or greater. The guinea pig injected with resuspended blood cells exhibited a febrile course from the eighth to thirteenth day—40.4° C., 39.9° C., 40.6° C., 40.3° C., and 39.9° C., respectively. A blood sample taken on the 24th day was positive for Q fever in a dilution of 1:64 or greater.

All four animals injected with bone-marrow suspension exhibited only low febrile courses, but on the 24th day results of the complement fixation test of the blood of each were positive for Q fever at dilutions of 1:64 or greater. Rickettsiae were observed in smears of exudate aspirated from the cutaneous lesion of one of these animals.

These experimental guinea pigs had been kept in cans in a small laboratory room where other guinea pigs infected with Q fever were present. Control animals were not kept in the same cans but 32 control guinea pigs were kept in the same animal room concurrently with these tests. All were bled and tested for antibodies after 30 days and the tests were negative for Q fever in all the 32 controls.

Tissues from an experimental animal in this series were sent to the Rocky Mountain Laboratory at Hamilton, Montana, and to the National Institute of Health laboratory at Bethesda, Maryland, and both reported the successful establishment of strains of *C. burneti* (Derrick) in guinea pigs by injection of these tissues. (The complement fixation tests reported herein were also made at these laboratories.)

SUMMARY

The first confirmed fatal case of Q fever in Los Angeles County is reported. The patient's occupation brought him in frequent contact with livestock (a characteristic of about 72 per cent of the cases so far studied in Southern California). The clinical course was typical of the disease. The patient was the first under 50 years of age known to have died of Q fever. The clinical history and the gross and microscopic pathological findings were consistent with those of a previous fatal case in America. The diagnosis was confirmed by the isolation of *C. burneti* in experimental animals injected with blood and sternal marrow collected at postmortem examination.

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Another death possibly due to Q fever: A patient who may have had Q fever died at the Los Angeles General Hospital in June, 1947. A blood sample taken late in the course of illness was sent to the National Institute of Health and the result of complement fixation test was positive for Q fever at a titer of 1:128 or greater.

When a report on this test was received at the Q fever laboratory, it was learned upon inquiry that the patient had died. An autopsy had been performed and a diagnosis of Hodgkin's disease made by the pathologist. The antibodies for Q fever may have been evidence of a previous illness. However, a review of the case suggests the patient was ill with Q fever at the time of death, and the high titer observed suggests recent infection with that disease.